Access DB# 119634

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Edward Woo Examiner #: 67450 Date: April 18, 2004
Art Unit: 1654 Phone Number 305-272-0588 Serial Number: 10/766392
Mail Box and Bldg/Room Location: 3014 Remsen Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. ME1

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Lee, Hyong Woo

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

RECEIVED
APR 19 2004
(STIC)

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Point of Contact: Alexandra Waclawiw	NA Sequence (#)	STN 8325
Searcher Phone: Technical Info. Specialist OM1 6A02 Tel: 308-4491	AA Sequence (#)	Dialog
Searcher Location: Rm 1A71 2-2534	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 4-19-04	Bibliographic	Dr.Link
Date Completed: 4-19-04	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 14	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: 35	Other	Other (specify)

PTO-1590 (8-01)

28

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 119634

TO: Edward Ward Location: REM/3D14/3D11 Art Unit: 1654 Monday, April 19, 2004 Case Serial Number: 10/600392	From: Alex Waclawiw Location: Biotech-Chem Library Rem 1A71 Phone: 272-2534 Alexandra.waclawiw@uspto.gov

Search Notes

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 APR 2004  HIGHEST RN 676118-37-9
DICTIONARY FILE UPDATES:  18 APR 2004  HIGHEST RN 676118-37-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
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http://www.cas.org/ONLINE/DBSS/registryss.html

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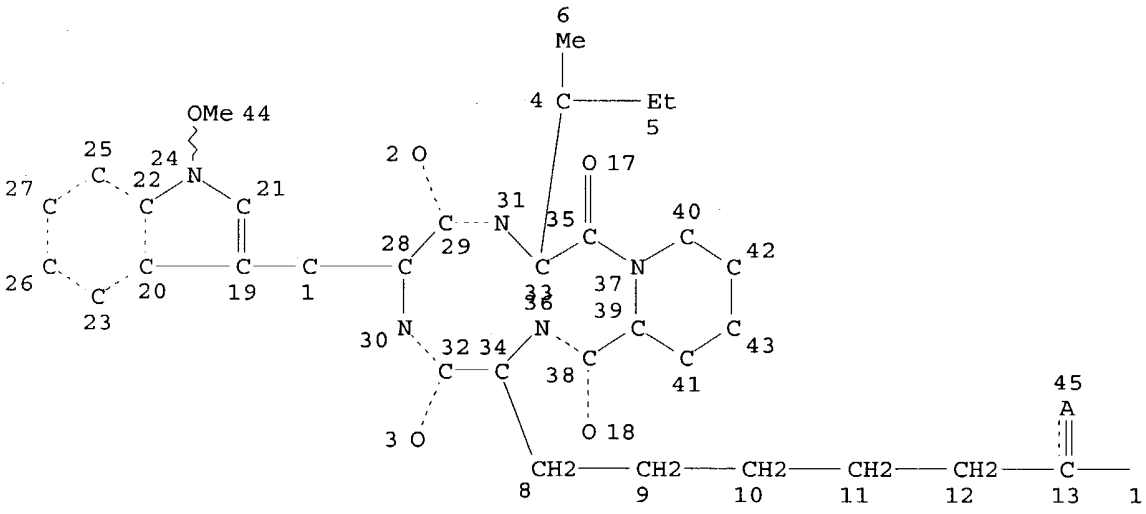

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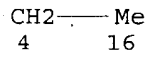

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 43

STEREO ATTRIBUTES: NONE
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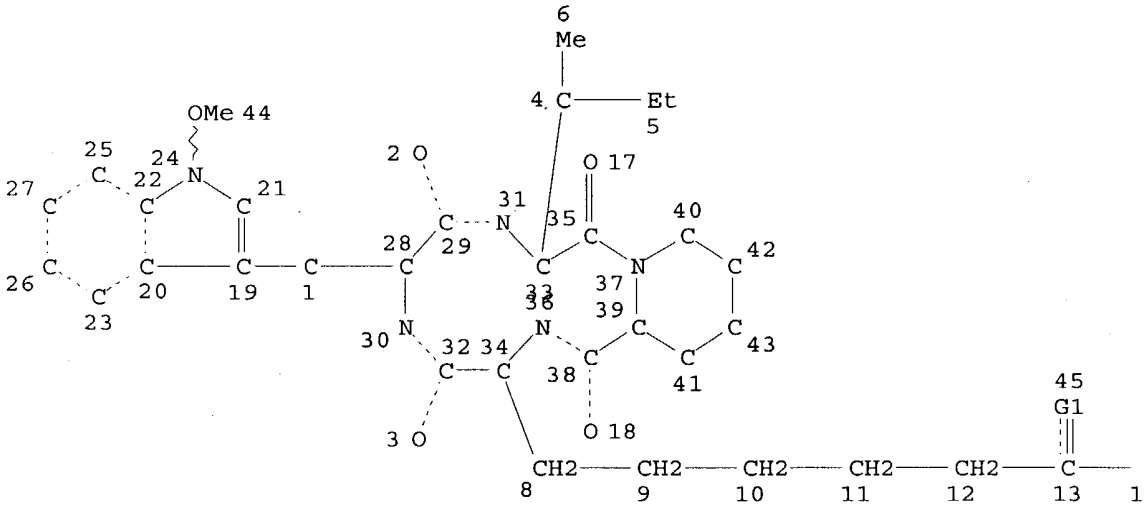

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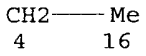

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STEREO ATTRIBUTES: NONE
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 Apr 2004 VOL 140 ISS 17
FILE LAST UPDATED: 18 Apr 2004 (20040418/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L9 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319478 CAPLUS
DOCUMENT NUMBER: 138:287984
TITLE: Preparation of apicidin-derived cyclic tetrapeptides
INVENTOR(S): Meinke, Peter T.; Schmatz, Dennis; Myers, Robert W.; Rattray, Sandra J.; Colletti, Steven L.; Wyvratt, Matthew J.; Fisher, Michael H.; Gurnett, Anne M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 104 pp., Cont.-in-part of U.S. Ser. No. 614,793.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003078369	A1	20030424	US 2002-66451	20020131

PRIORITY APPLN. INFO.: US 1999-145329P P 19990723
US 2000-614793 A2 20000712
OTHER SOURCE(S): MARPAT 138:287984
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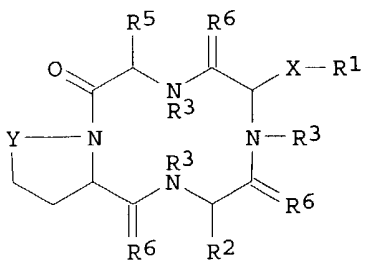

I

AB Cyclic tetrapeptide compds. I [X = CH2, CO, CHOH, alkoxy- or aryloxymethylene, etc., :CH, or not present; Y = (CH2)n, where n = 1 or 2; R1 = H, alkyl, aryl, acyl, CN, CO2H or ester, carboxamido, etc.; R2 = (un)substituted alkyl, alkenyl, or alkynyl, alkoxy, alkoxyalkyl; R3 = H, halo, OH, alkoxy, aryloxy, etc., alkyl, aryl; R5 = iso-Pr, sec-butyl; R6 = O, S, H2 (with provisos)] derived from apicidin were prepared for therapeutic inhibition of histone deacetylase activity. Thus, treating 300 mg apicidin with 18 mg NaBH4 in MeOH and stirring 4 h at room temperature afforded carbonyl reduction product cyclo(N-O-methyl-L-Trp-L-Ile-D-Pip-L-2-amino-8-hydroxydecanoyl) (pip = pipecolic acid residue).

IC ICM C07K007-54
ICS C07D245-00

NCL 530317000; 540460000

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7

IT 189337-30-2P 189337-32-4P 312956-80-2P 312956-81-3P 312956-82-4P
312956-83-5P 312956-86-8P 312956-88-0P 312956-90-4P 312956-91-5P
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322002-18-6P 322411-12-1P 322411-13-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of apicidin-derived cyclic tetrapeptides)

IT **314058-20-3P 322000-66-8P 322000-67-9P**
322001-77-4P 322001-78-5P 322001-79-6P
322001-80-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of apicidin-derived cyclic tetrapeptides)

RN 314058-20-3 CAPLUS

CN Cyclo[(2S)-2-amino-8-methylenedecanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

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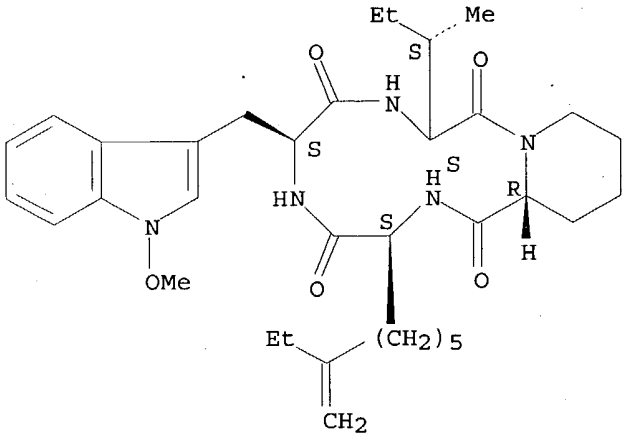
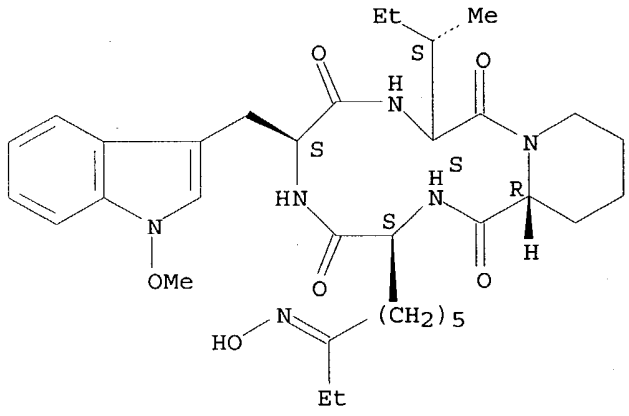


RN 322000-66-8 CAPLUS
CN Cyclo[(2S)-2-amino-8-(hydroxyimino)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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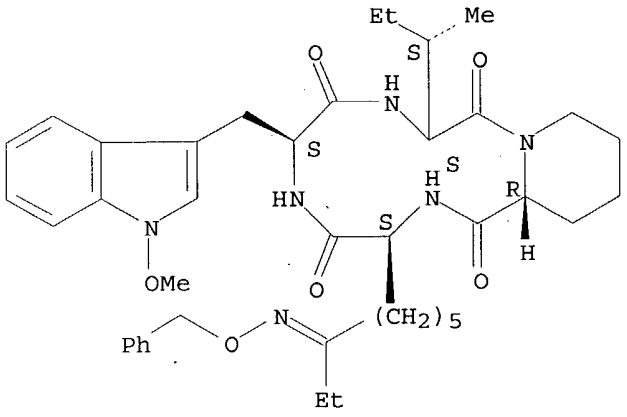
CN Cyclo[(2S)-2-amino-8-[(phenylmethoxy)imino]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 322001-77-4 CAPLUS
CN Cyclo[(2S)-2-amino-8-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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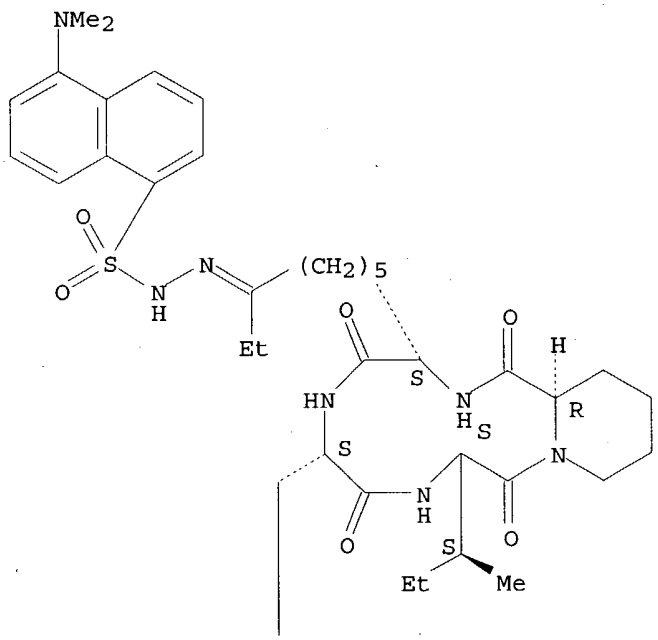

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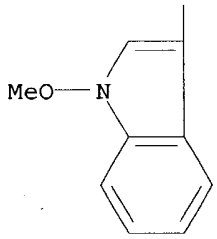

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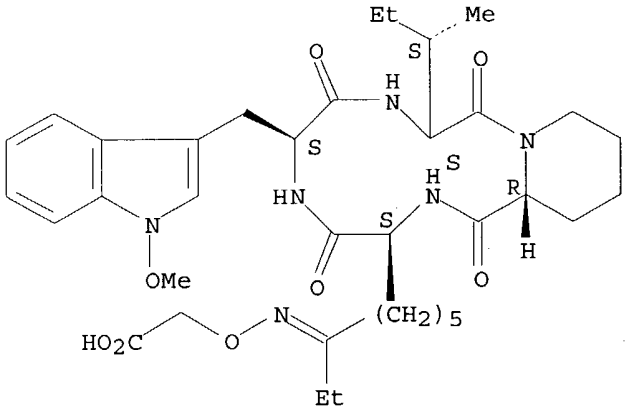
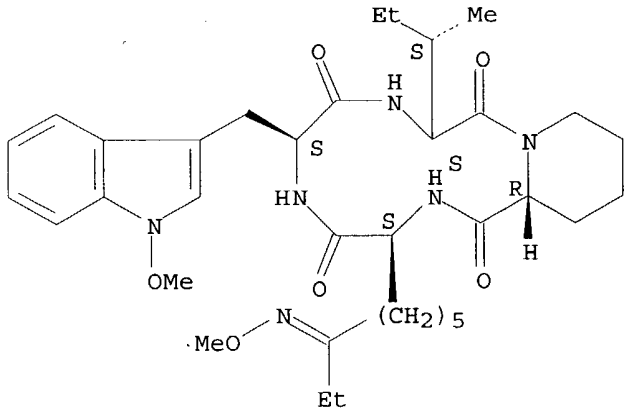
CN Cyclo[(2S)-2-amino-8-[(carboxymethoxy)imino]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 322001-79-6 CAPLUS
CN Cyclo[(2S)-2-amino-8-(methoxyimino)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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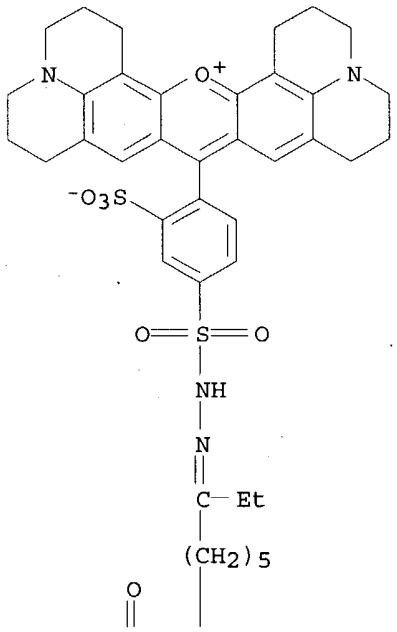
PAGE 1-A



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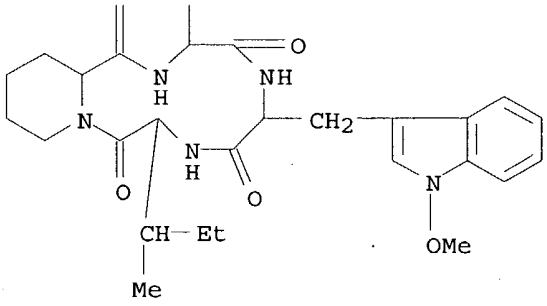

L9 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:504791 CAPLUS
DOCUMENT NUMBER: 137:79231
TITLE: Preparation and formulation of apicidin derivatives for use as antitumor agents
INVENTOR(S): Lee, Hyang Woo; Jung, Young Hoon; Han, Jeung Whan; Lee, Seok Yong; Lee, Yin Won; Lee, Hoi Young; Zee, Ok

	Pyo
PATENT ASSIGNEE(S):	S. Korea
SOURCE:	PCT Int. Appl., 24 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051846	A1	20020704	WO 2001-KR2228	20011221
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004014647	A1	20040122	US 2003-600392	20030620

PRIORITY APPLN. INFO.:	KR 2000-80180	A	20001222
	WO 2001-KR2228	A1	20011221

OTHER SOURCE(S): CASREACT 137:79231; MARPAT 137:79231

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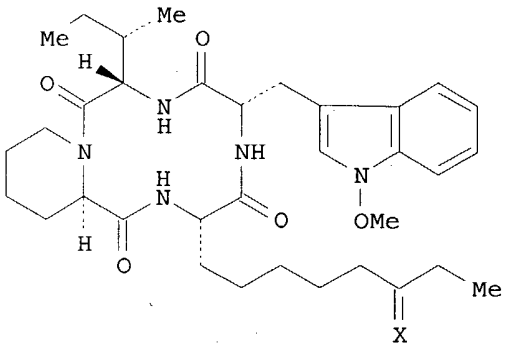

I

AB Apicidin derivs. I [X = semicarbazone, thiosemicarbazone, hydrazone, tert-butylhydrazone, phenylhydrazone, 2,4-dinitrophenylhydrazone, 4-methoxyphenylhydrazone, 3-methoxyphenylhydrazone, 4-nitrophenylhydrazone, benzylhydrazone, methanesulfonylhydrazone, benzenesulfonylhydrazone, 4-methylbenzenezulfonylhydrazone, benzoylhydrazone, 4-nitrobenzoylhyrazone, carbohydrazone, benzyloxime, acetoxime] were prepared for pharmaceutical use in the treatment of cancer. Thus, apicidin Ia I (X = O), which was obtained via a fermentation process, was reacted with semicarbazide hydrochloride using Et3N in methanol to give apicidin Ia semicarbazone I (X = NNHCONH2) in 85.3% yield. The prepared apicidin derivs. were tested for inhibition of histone deacetylase and growth of cancer cells.

IC ICM C07D487-04

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 16, 63

IT **322000-66-8P**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and formulation of apicidin derivs. for use as antitumor agents)

IT **322000-67-9P 439859-08-2P**, Apicidin Ia semicarbazone
439859-09-3P 439859-10-6P 439859-11-7P
439859-12-8P 439859-13-9P 439859-14-0P
439859-15-1P 439859-16-2P 439859-17-3P
439859-18-4P 439859-19-5P 439859-20-8P
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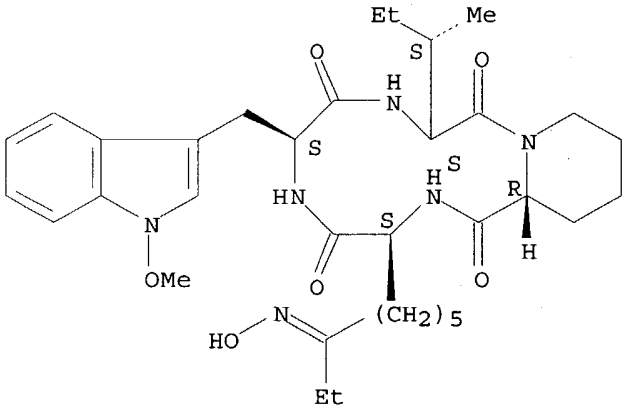
439859-24-2P
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of apicidin derivs. for use as antitumor agents)

IT **322000-66-8P**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and formulation of apicidin derivs. for use as antitumor agents)

RN 322000-66-8 CAPLUS

CN Cyclo[(2S)-2-amino-8-(hydroxyimino)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT **322000-67-9P 439859-08-2P**, Apicidin Ia semicarbazone
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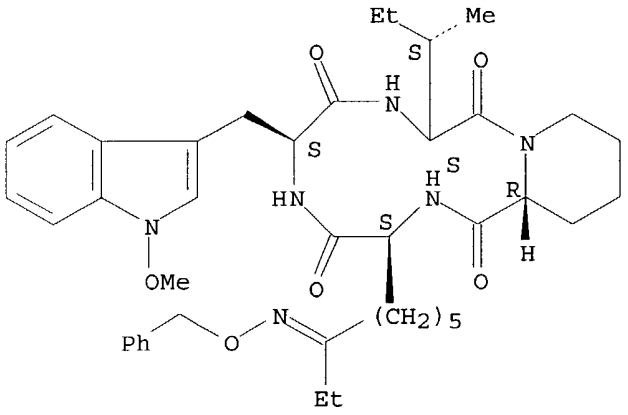
439859-24-2P
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);

PREP (Preparation); USES (Uses)
(preparation and formulation of apicidin derivs. for use as antitumor agents)

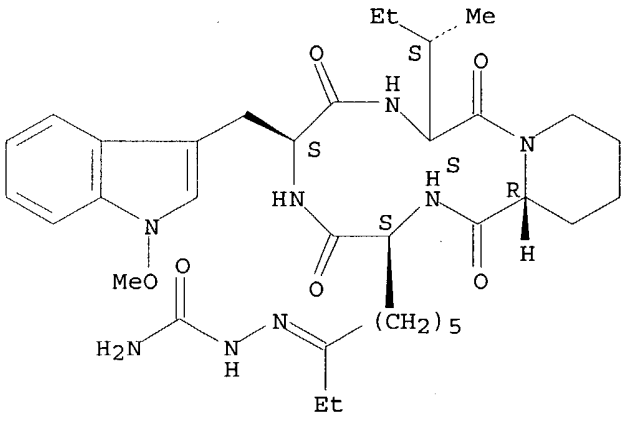
RN 322000-67-9 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(phenylmethoxy)imino]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



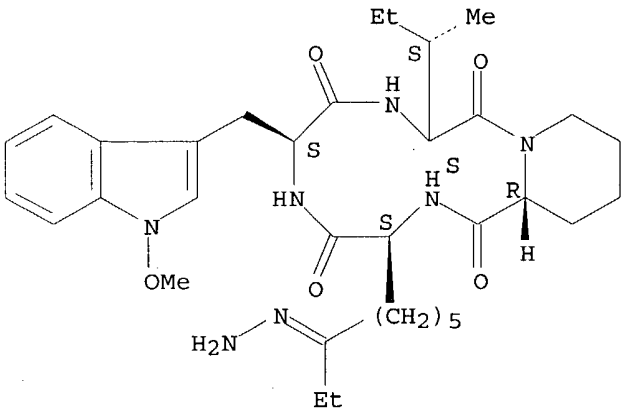
RN 439859-08-2 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(aminocarbonyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



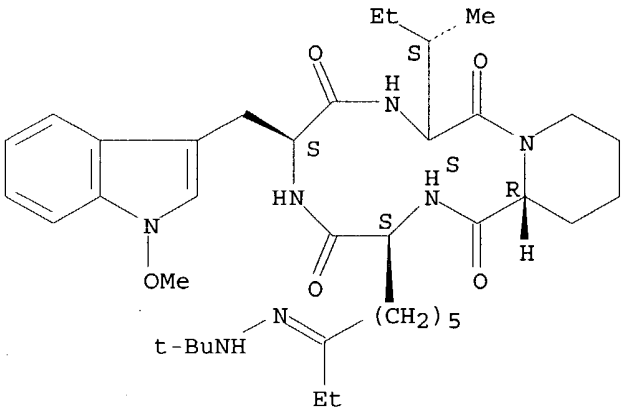
RN 439859-09-3 CAPLUS
CN Cyclo[(2S)-2-amino-8-hydrazonodecanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



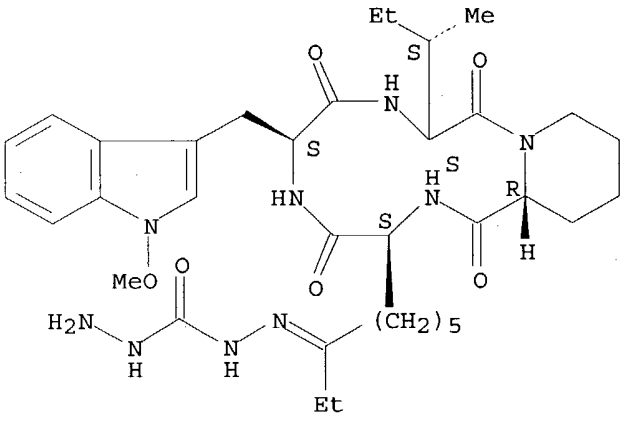
RN 439859-10-6 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(1,1-dimethylethyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



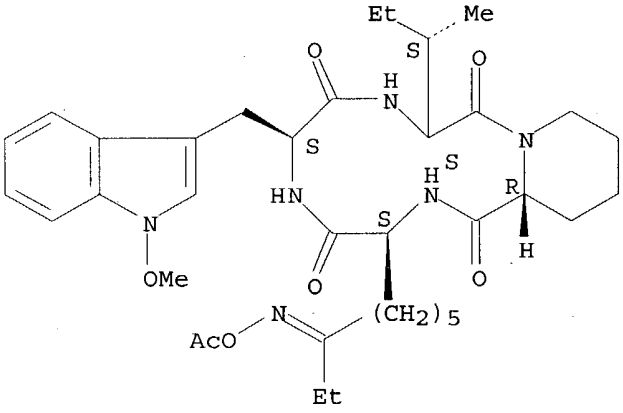
RN 439859-11-7 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(hydrazinocarbonyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



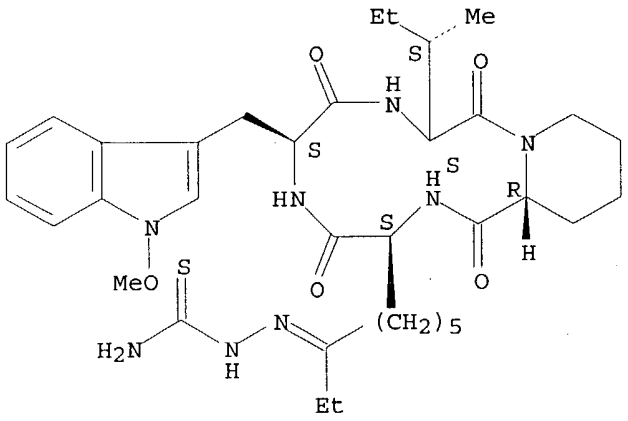
RN 439859-12-8 CAPLUS
CN Cyclo[(2S)-8-[(acetyloxy)imino]-2-aminodecanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



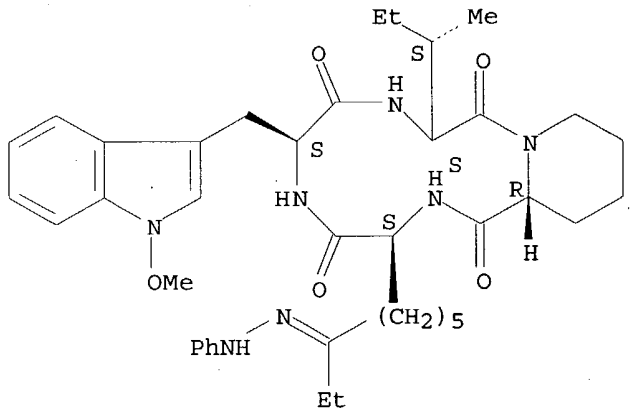
RN 439859-13-9 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(aminothioxomethyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



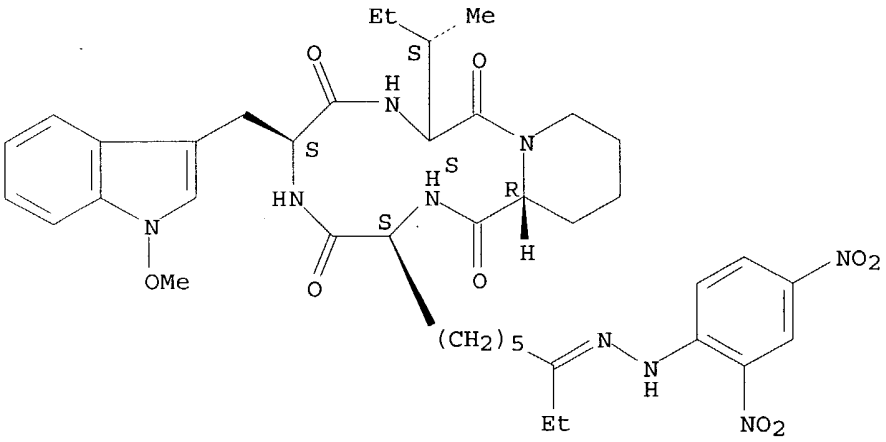
RN 439859-14-0 CAPLUS
CN Cyclo[(2S)-2-amino-8-(phenylhydrazono)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



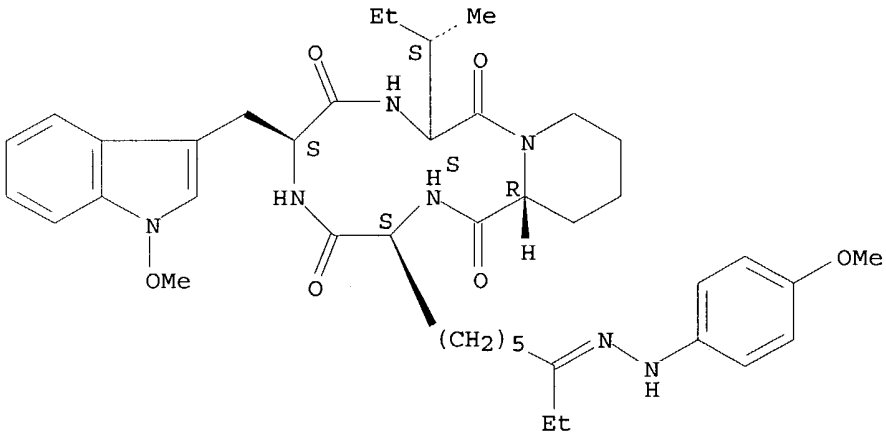
RN 439859-15-1 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(2,4-dinitrophenyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



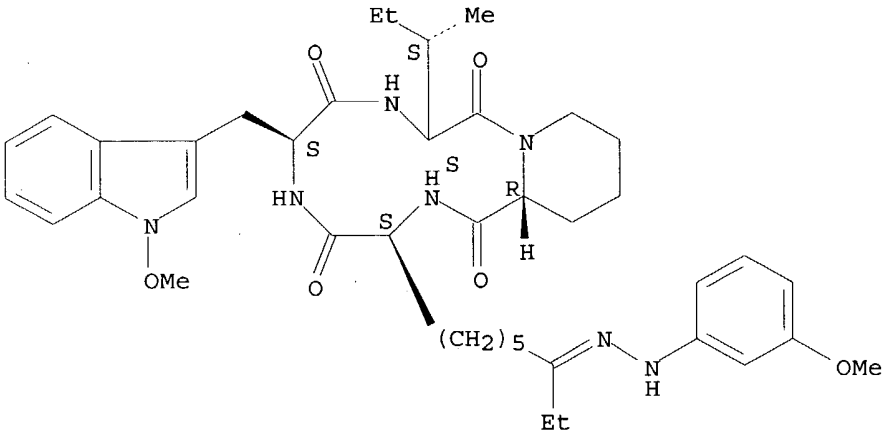
RN 439859-16-2 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(4-methoxyphenyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



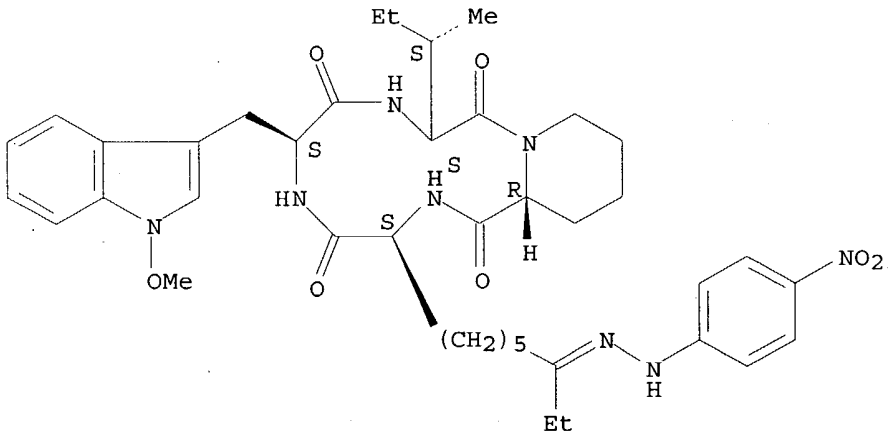
RN 439859-17-3 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(3-methoxyphenyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



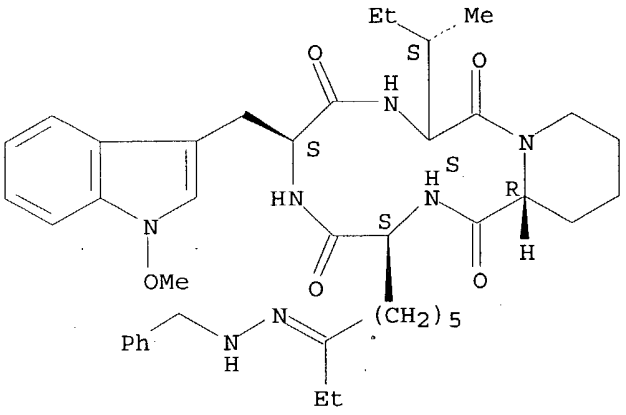
RN 439859-18-4 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(4-nitrophenyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



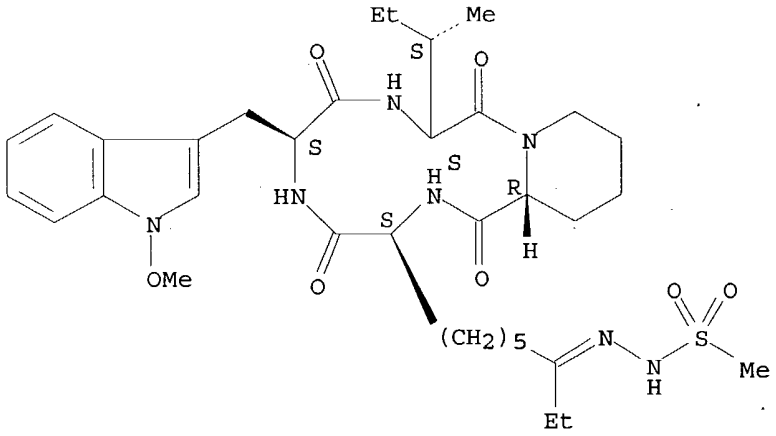
RN 439859-19-5 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(phenylmethyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



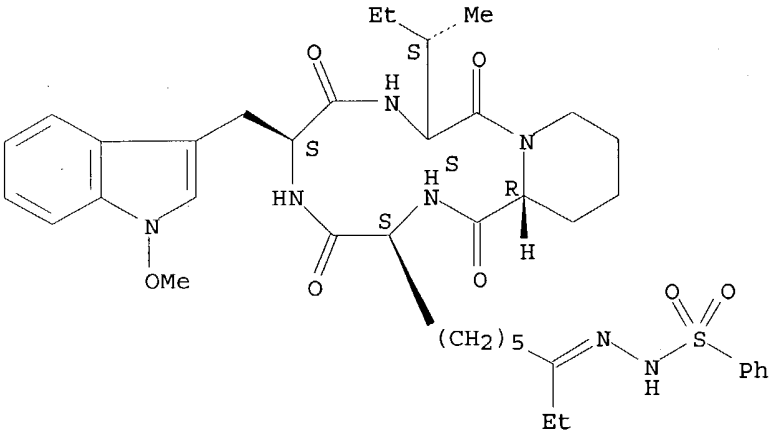
RN 439859-20-8 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(methylsulfonyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



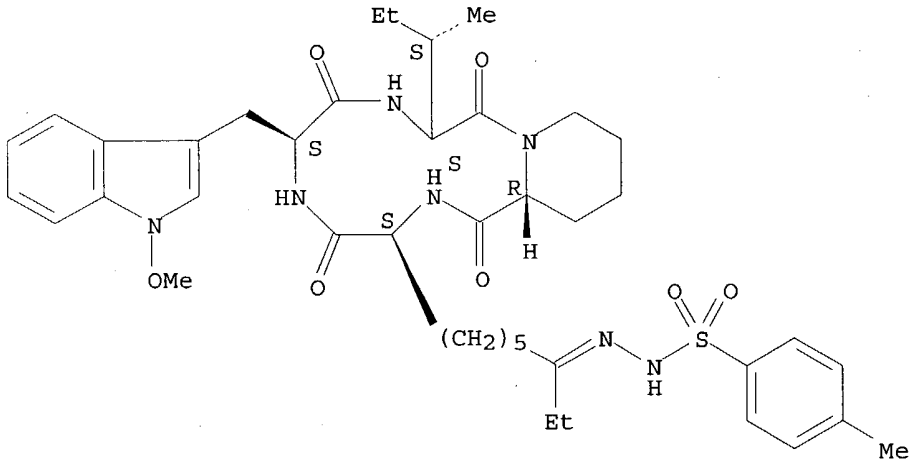
RN 439859-21-9 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(phenylsulfonyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



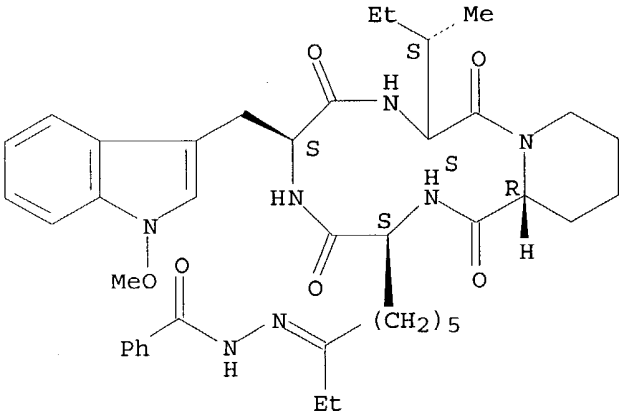
RN 439859-22-0 CAPLUS
CN Cyclo[(2S)-2-amino-8-[[(4-methylphenyl)sulfonyl]hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



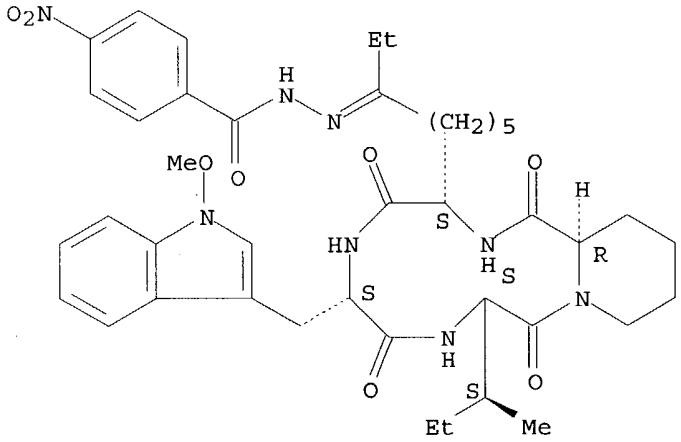
RN 439859-23-1 CAPLUS
CN Cyclo[(2S)-2-amino-8-(benzoylhydrazono)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439859-24-2 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(4-nitrobenzoyl)hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

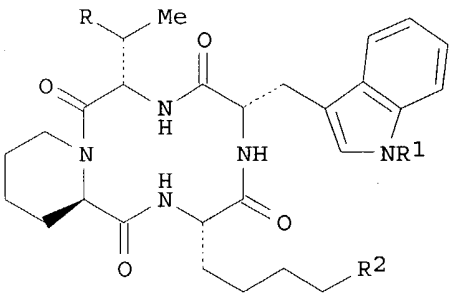
Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:34206 CAPLUS
DOCUMENT NUMBER: 136:232540
TITLE: Structure and Chemistry of Apicidins, a Class of Novel Cyclic Tetrapeptides without a Terminal α-Keto Epoxide as Inhibitors of Histone Deacetylase with Potent Antiprotozoal Activities
AUTHOR(S): Singh, Sheo B.; Zink, Deborah L.; Liesch, Jerrold M.; Mosley, Ralph T.; Dombrowski, Anne W.; Bills, Gerald F.; Darkin-Rattray, Sandra J.; Schmatz, Dennis M.; Goetz, Michael A.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Organic Chemistry (2002), 67(3), 815-825
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:232540
GI



I

AB Apicidins I [R = Et, R1 = OMe, R2 = CH2COEt; R = Et, R1 = H, R2 = CH2COEt; R = Me, R1 = OMe, R2 = CH2COEt; R = Et, R1 = OMe, R2 = CH2COCH(OH)Me; R = Et, R1 = OMe, R2 = CH2CH(S-OH)Et; R = Et, R1 = OMe, R2 = CH2CH2CH(OH)Me] are a class of cyclic tetrapeptides that do not contain the classical electrophilic α-keto epoxide and yet are potent (nM) inhibitors of histone deacetylase and antiprotozoal agents. I showed broad-spectrum activities against the apicomplexan family of protozoa including Plasmodium sp (malarial parasite), Toxoplasma gondii, Cryptosporidium sp., and Eimeria sp. These cyclic peptides contain a β-turn amino acid (R)-Pip or (R)-Pro, (S)-N-methoxytryptophan, (S)-Ile or (S)-Val, and either (S)-2-amino-8-oxodecanoic acid or a modified (S)-2-amino-8-oxodecanoic acid. The isolation and structure elucidation of new apicidins from two Fusarium species, temperature-dependent NMR studies of apicidin, NMR and mol. modeling based conformation of the 12-membered macrocyclic ring, and selected chemical modifications of apicidin have been detailed in this paper. The cyclic nature of the peptide, the C-8 keto group, and the tryptophan are all critical for the biol. activity.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7, 16

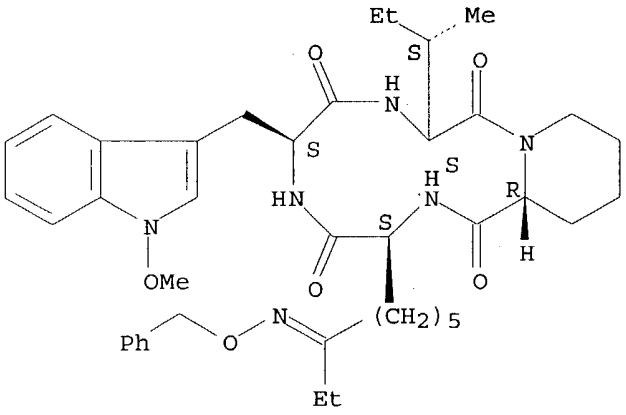
IT 314058-18-9P **322000-67-9P** 322000-72-6P 403501-69-9P
403501-70-2P 403501-71-3P 403501-72-4P 403501-73-5P 403501-74-6P
403501-75-7P 403501-76-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of apicidin derivs. as inhibitors of histone deacetylase with potent antiprotozoal activities)

IT **322000-67-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of apicidin derivs. as inhibitors of histone deacetylase with potent antiprotozoal activities)

RN 322000-67-9 CAPLUS

CN Cyclo[(2S)-2-amino-8-[(phenylmethoxy)imino]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

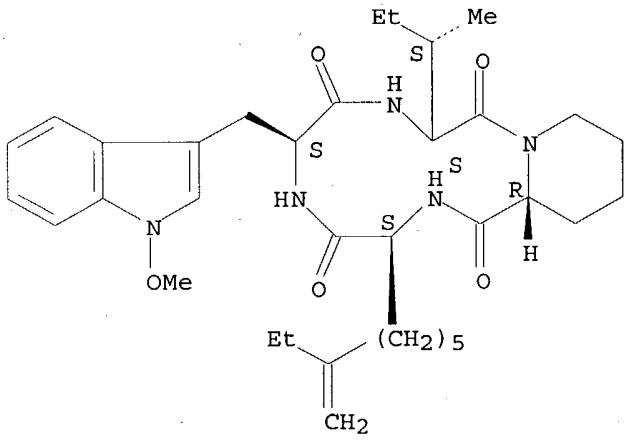
L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:83649 CAPLUS
DOCUMENT NUMBER: 134:289954
TITLE: Broad spectrum antiprotozoal agents that inhibit histone deacetylase: structure-activity relationships of apicidin. Part 1
AUTHOR(S): Colletti, S. L.; Myers, R. W.; Darkin-Rattray, S. J.; Gurnett, A. M.; Dulski, P. M.; Galuska, S.; Allocco, J. J.; Ayer, M. B.; Li, C.; Lim, J.; Crumley, T. M.; Cannova, C.; Schmatz, D. M.; Wyvratt, M. J.; Fisher, M. H.; Meinke, P. T.
CORPORATE SOURCE: Merck Research Laboratories, Merck & Co., Inc., Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(2), 107-111
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Apicidin, a natural product recently isolated at Merck, inhibits both mammalian and protozoan histone deacetylases (HDACs). The conversion of apicidin, a nanomolar inhibitor of HDACs, into a series of side-chain analogs that display picomolar enzyme affinity is described within this structure-activity study.
CC 1-3 (Pharmacology)
Section cross-reference(s): 7, 10, 26, 27
IT 312956-79-9 312956-84-6 312956-86-8 312956-88-0 312956-89-1
312956-90-4 312956-91-5 312956-92-6 312956-95-9 312956-96-0
312957-00-9 312957-01-0 312957-03-2 312957-04-3 314058-18-9
314058-19-0 **314058-20-3** 314058-23-6 314058-24-7
314058-25-8 314058-27-0 322000-77-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiprotozoal activity and histone deacetylase inhibition by apicidin analogs)
IT **314058-20-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(antiprotozoal activity and histone deacetylase inhibition by apicidin analogs)

RN 314058-20-3 CAPLUS

CN Cyclo[(2S)-2-amino-8-methylenedecanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:78233 CAPLUS

DOCUMENT NUMBER: 134:131817

TITLE: Preparation of apicidin-derived cyclic tetrapeptides

INVENTOR(S): Meinke, Peter T.; Schmatz, Dennis; Fisher, Michael H.; Rattray, Sandra J.; Colletti, Steven L.; Wyvratt, Matthew J.; Myers, Robert W.; Gurnett, Anne M.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 229 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

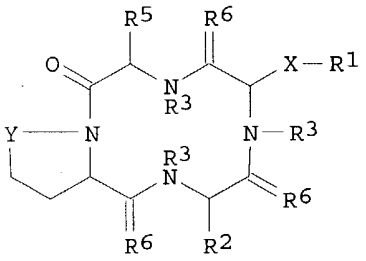
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007042	A1	20010201	WO 2000-US19627	20000719
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1204411	A1	20020515	EP 2000-947507	20000719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

JP 2003505417 T2 20030212 JP 2001-511926 20000719
PRIORITY APPLN. INFO.: US 1999-145329P P 19990723
WO 2000-US19627 W 20000719
OTHER SOURCE(S): MARPAT 134:131817
GI



I

AB Cyclic tetrapeptide compds. I [X = CH2, CO, CHOH, alkoxy- or aryloxymethylene, etc., :CH, or not present; Y = (CH2)n, where n = 1 or 2; R1 = H, alkyl, aryl, acyl, CN, CO2H or ester, carboxamido, etc.; R2 = (un)substituted alkyl, alkenyl, or alkynyl, (CH2)nii-O-(CH2)mii, where nii, mii = 0-7; R3 = H, halo, OH, alkoxy, aryloxy, etc., alkyl, aryl; R5 = iso-Pr, sec-butyl; R6 = O, S, H2 (with provisos)] derived from apicidin were prepared for therapeutic inhibition of histone deacetylase activity. Thus, treating 300 mg apicidin with 18 mg NaBH4 in MeOH and stirring 4 h at room temperature afforded carbonyl reduction product cyclo(N-O-methyl-L-Trp-L-Ile-D-Pip-L-2-amino-8-hydroxydecanoyl) (pip = pipecolic acid residue).

IC ICM A61K031-395
ICS A61K038-12; C07D257-10; C07K005-12

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7

IT 189337-30-2P 189337-32-4P 312956-80-2P 312956-81-3P 312956-82-4P
312956-83-5P 312956-86-8P 312956-88-0P 312956-90-4P 312956-91-5P
312956-92-6P 312956-95-9P 312956-96-0P 312956-97-1P 312957-00-9P
312957-05-4P 314058-15-6P 314058-18-9P 314058-19-0P
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314058-27-0P 315189-83-4P 315189-84-5P 315189-87-8P 315189-92-5P
315189-93-6P 315189-94-7P 315189-95-8P 315189-96-9P 315189-97-0P
315189-99-2P 315190-03-5P 315190-04-6P 315190-05-7P 315190-06-8P
315190-07-9P 315190-11-5P 315190-12-6P 315190-13-7P 315190-14-8P
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322000-66-8P **322000-67-9P** 322000-68-0P 322000-69-1P
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322000-99-7P 322001-00-3P 322001-01-4P 322001-03-6P 322001-05-8P
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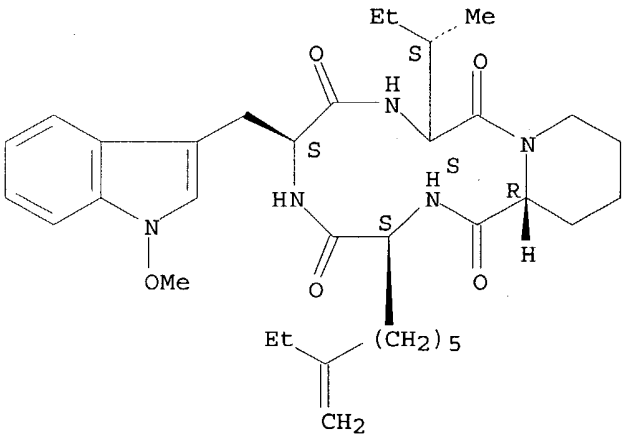
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of apicidin-derived cyclic tetrapeptides)

IT **314058-20-3P 322000-66-8P 322000-67-9P**
322001-77-4P 322001-78-5P 322001-79-6P
322001-80-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of apicidin-derived cyclic tetrapeptides)

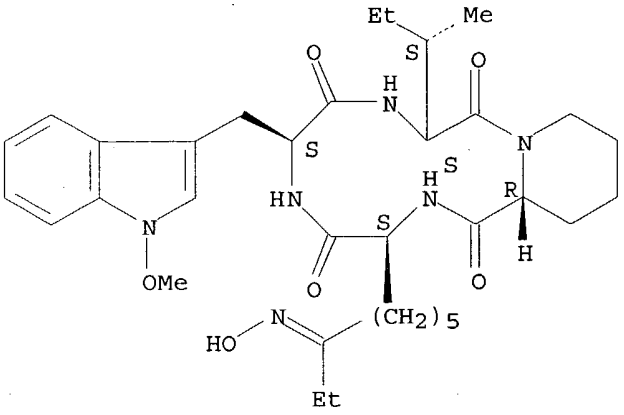
RN 314058-20-3 CAPLUS
CN Cyclo[(2S)-2-amino-8-methylenedecanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



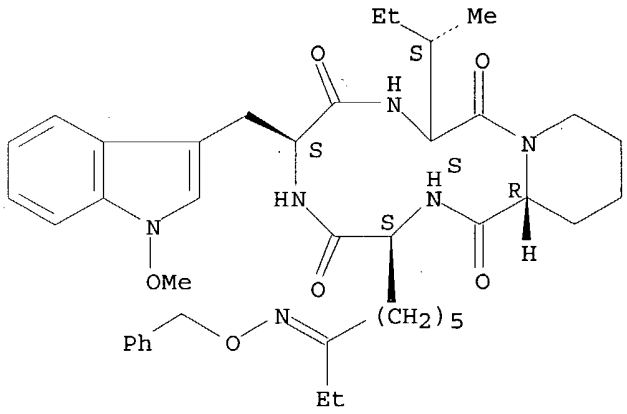
RN 322000-66-8 CAPLUS
CN Cyclo[(2S)-2-amino-8-(hydroxyimino)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 322000-67-9 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(phenylmethoxy)imino]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 322001-77-4 CAPLUS
CN Cyclo[(2S)-2-amino-8-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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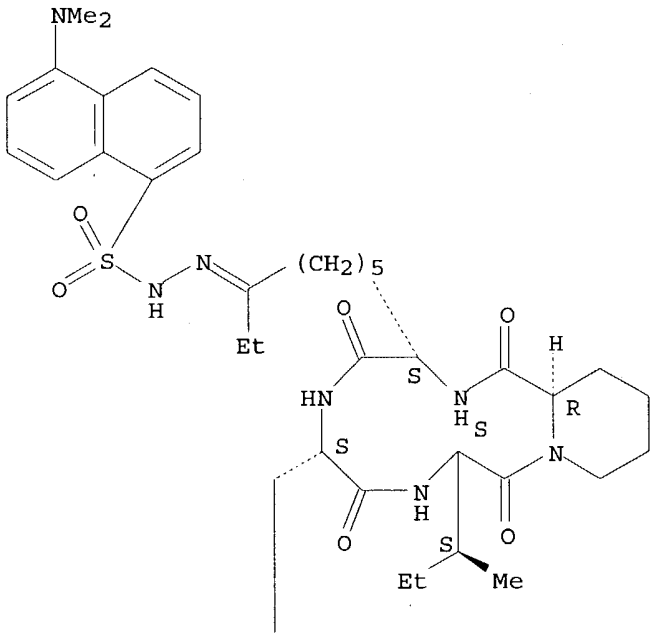

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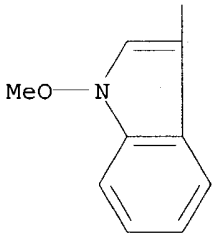
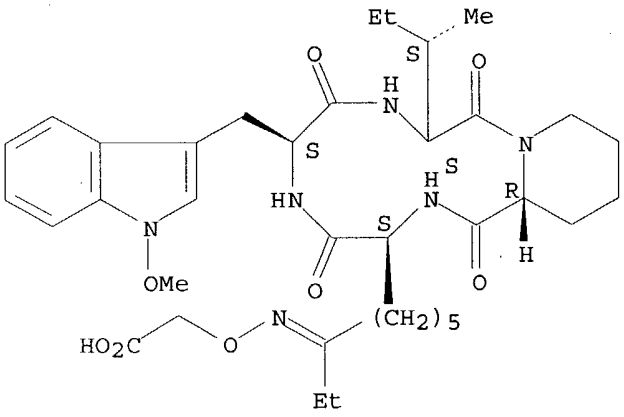


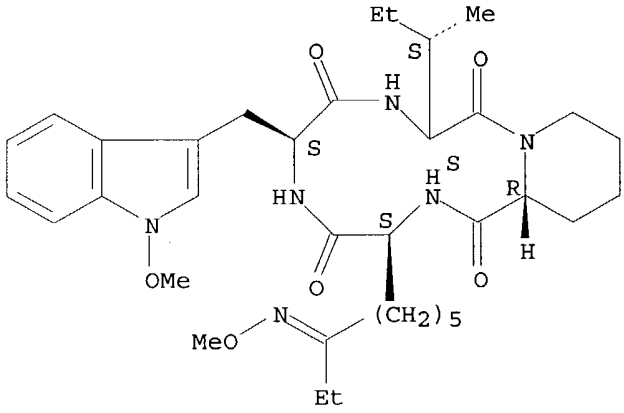
RN 322001-78-5 CAPLUS
CN Cyclo[(2S)-2-amino-8-[(carboxymethoxy)imino]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



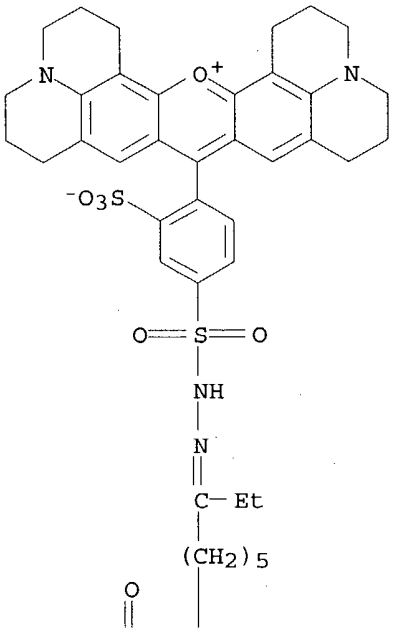
RN 322001-79-6 CAPLUS
CN Cyclo[(2S)-2-amino-8-(methoxyimino)decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 322001-80-9 CAPLUS
CN Cyclo[(2S)-2-amino-8-[[[4-(2,3,6,7,12,13,16,17-octahydro-1H,5H,11H,15H-xantheno[2,3,4-ij:5,6,7-i'j']diquinolizin-18-ium-9-yl)-3-sulfophenyl]sulfonyl]hydrazono]decanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl], inner salt (9CI) (CA INDEX NAME)

PAGE 1-A



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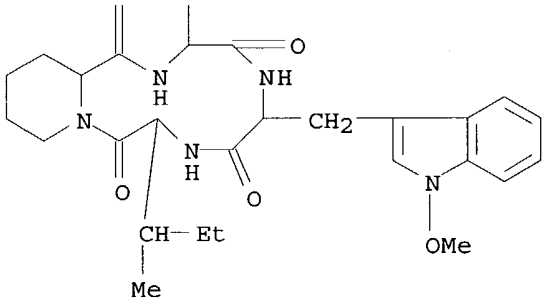


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:805815 CAPLUS
DOCUMENT NUMBER: 134:56953
TITLE: Design and synthesis of histone deacetylase inhibitors: the development of apicidin transition state analogs
AUTHOR(S): Colletti, Steven L.; Myers, Robert W.; Darkin-Rattray, Sandra J.; Schmatz, Dennis M.; Fisher, Michael H.; Wyvratt, Matthew J.; Meinke, Peter T.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Merck and Co., Inc., Rahway, NJ, 07065, USA

SOURCE: Tetrahedron Letters (2000), 41(41), 7837-7841
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:56953

AB A four step degradation of the C8 Et ketone of apicidin provided a route to the C6 aldehyde intermediate and several mechanism-based transition state inhibitors of histone deacetylase. The compds. generated herein delineate the significance of apicidin's side chain, highlighted by the high affinity C8 aldehyde and C8-keto-9,10-epoxide analogs of apicidin.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

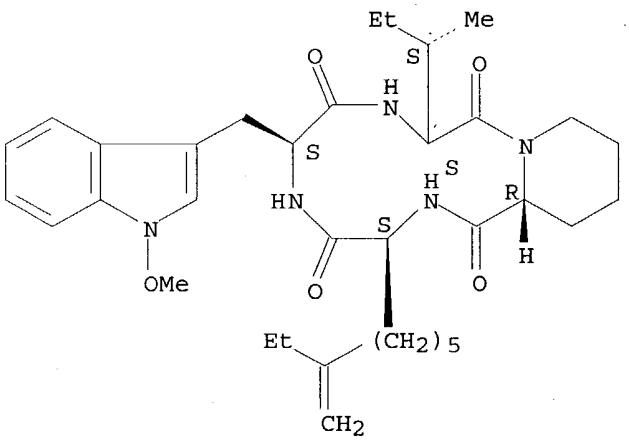
IT 312956-88-0P 312956-97-1P 314058-18-9P 314058-19-0P
314058-20-3P 314058-23-6P 314058-24-7P 314058-26-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of apicidin transition state analogs as histone deacetylase inhibitors)

IT **314058-20-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of apicidin transition state analogs as histone deacetylase inhibitors)

RN 314058-20-3 CAPLUS

CN Cyclo[(2S)-2-amino-8-methylenedecanoyl-1-methoxy-L-tryptophyl-L-isoleucyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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